IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Kogami et al.
Appl. No.	:	10/523,287
Filed	:	February 3, 2005
For	:	PROCESS FOR PRODUCING N-MONOALKYL-3-HYDROXYL-3-(2-THIENYL) PROPANAMINE AND INTERMEDIATE
Examiner	:	Robert H. Havlin
Group Art Unit	:	1626

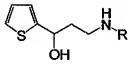
DECLARATION UNDER 37 C.F.R. 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

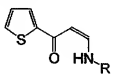
I, SATAKE Syuzo, declare and state:

1 I am one of the co-inventors of the invention claimed in the above-identified application and am familiar with the specification, claims, and prosecution history thereof. These claims are directed to a processes for producing an N-monoalkyl-3-hydroxy-3-(2-thienyl)propanamine represented by General Formula (2):



(2)

wherein R is C_{1-4} alkyl, comprising the step of reducing a (*Z*)-*N*-monoalkyl-3-oxo-3-(2-thienyl)propenamine represented by General Formula (1):



(1)

wherein R is as defined above. The claims also are directed to the starting compound, a (*Z*)-*N*-monoalkyl-3-oxo-3-(2-thienyl)propenamine represented by General Formula (1).

2 I have read the Office Actions mailed April 24, 2007 and October 18, 2007, and understand that Claims 4 and 5 have been rejected under 35 U.S.C. § 103(a), as being obvious in view of methyl analogs disclosed in Cassella Farbwerke et al. (CA 88:105153); Singh et al., (CA 115:29157); and Bogdanowicz-Swed et al. (CA 136:118356).

3. N-monoalkyl-3-hydroxy-3-(2-thienyl)propanamine represented by General Formula (2) of instant Claim 1 is useful as a medicinal intermediate, and therefore the (*Z*)-N-monoalkyl-3-oxo-3-(2-thienyl)propenamines of Claims 4 and 5 are process intermediates useful in the preparation of the propanamine of Claim 1 and can produce results that are functionally quite different from the three prior art compounds cited by the Examiner.

4. "CHIRALITY, 12, 26-29(2000)", which is mentioned in the instant specification as one of the prior art references under the title of BACKGROUND ART, discloses a process in the preparation of Duloxetine (an antidepressant). CHRALITY also discloses that Duloxetine, which is an (S)-form compound, can be prepared from (*S*)-3-methylamino-1-(2-thienyl)-1-propanol ((S)-6) (see page 27, Fig. 1 and page 27, right column, to page 28, left column). A copy of CHIRALITY was submitted with the IDS filed April 21, 2005.

5. The (*S*)-3-methylamino-1-(2-thienyl)-1-propanol disclosed in CHIRALITY is an S-isomer of N-methyl-3-hydroxy-3-(2-thienyl)propanamine, which is a methyl analog of N-monoalkyl-3-hydroxy-3-(2-thienyl)propanamine, i.e., a propanamine when R is a methyl in General Formula (2) of instant Claim 1.

6. It is commonly known in the art that S-isomers can be separated from a racemic mixture (racemate) containing both *S*-isomers and *R*-isomers by column separation or a like method using high-performance liquid chromatography. Therefore, (*S*)-N-methyl-3-hydroxy-3-(2-thienyl)propanamine (corresponding to (S)-3-methylamino-1-(2-thienyl)-1-propanol) can be easily obtained from N-methyl-3-hydroxy-3-(2-thienyl)propanamine.

7. Accordingly, the (Z)-N-monoalkyl-3-oxo-3-(2-thienyl)propenamines in instant Claims 4 and 5 are useful as preparation materials for (S)-N-methyl-3-hydroxy-3-(2-thienyl)propanamine (i.e., (S)-3-methylamino-1-(2-thienyl)-1-propanol), which is a useful intermediate in the preparation of Duloxetine (an antidepressant).

8. Compound [2] in the enclosed Exhibit A is 3-amino-1-(2-thienyl)-2-propen-1-one disclosed in Cassella Farbwerke et al. Compound [3] indicates 3-amino-1-(2-thienyl)-2-buten-1-

one disclosed in Singh et al. Compound [4] shows 3-dimethyl-1-(2-propen-1-one of Bogdanowicz-Swed et al. By comparing the structural formulae, it becomes very clear that the Compounds [2] to [4] disclosed in the three prior art references cannot be used as a material for directly obtaining N-monoalkyl-3-hydroxy-3-(2-thienyl)propanamine.

9. The Examiner's rejection on the basis that the (Z)-N-monoalkyl-3-oxo-3-(2-thienyl)propenamines recited in Claims 4 and 5 produce or posess the same or similar results or properties as those of the compounds disclosed in the three references is groundless. On the contrary, the propenamines of Claims 4 and 5 achieve results that are distinct from the compounds disclosed in the three references. Accordingly, the subject matter of Claims 4 and 5 is unobious over the cited references.

11. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful, false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 2008.01.24 Satake Syuzo
SATAKE Syuzo

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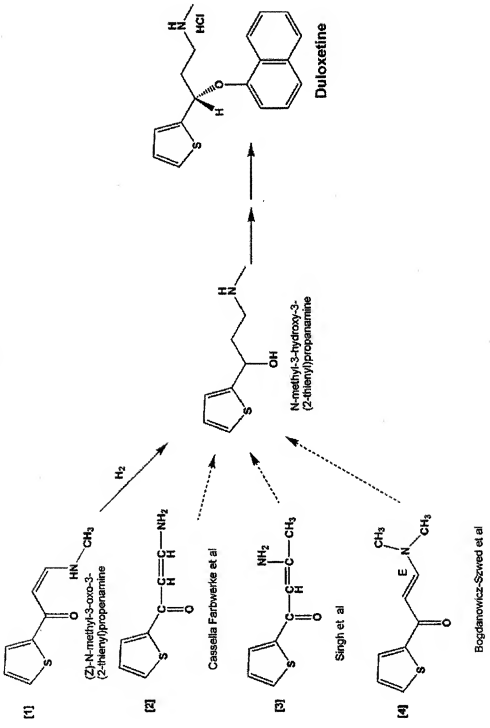
EXHIBIT A

Fig. 1


[1]
(Z)-N-methyl-3-oxo-3-(2-thienyl)propanamine
[2]
Cassella Farbwerke et al
[3]
Singh et al
[4]
Bogdanowicz-Szwed et al
H2
N-methyl-3-hydroxy-3-(2-thienyl)propanamine
Duloxetine
HCl